REMARKS

Claims 1-4, 6, 8, and 10-29 are currently pending. Claims 8, 10-13, 17-28 are withdrawn and 5, 7, 9, 29, and 30 are cancelled.

Claim 1 was amended to correct typographical errors and to expedite prosecution on the merits in view of the enablement rejection of claims 1, 6, and 29. Claims 2 and 3 were amended to expedite prosecution on the merits in view of the claim objection and the indefiniteness rejections. Claim 29 was cancelled without prejudice with Applicants reserving full rights to re-introduce the subject matter in this or another claiming the benefit of priority to the captioned application. It is submitted that no new matter has been added by the above amendments. Entry of the amendments and allowance of the claims is respectfully requested.

Objection to the Claims

Claim 1 was objected to for certain typographical errors. (Office Action at page 2.) The offending language has been cancelled from claim 1. It is submitted that the objection is moot and should be withdrawn.

The Patent Office requested insertion of "or" before (c-11) in claim 11. That word has been added and the objection has been overcome. Therefore the objection should be withdrawn.

Claims 2-3 were objected to under 37 CFR § 1.75 (c) for being improper dependent form. (Office Action at page 2). Claims 2-3 have been amended to overcome this objection. Withdrawal thereof is respectfully requested

Indefiniteness Rejection

Claims 2-3 were rejected under 35 USC §112, second paragraph. (Office Action at page 3). Claims 203 have been amended to delete (c-2). With this amendment, it is believed the rejection is moot and should be withdrawn.

Enablement Rejection

Claims 1, 6, and 29 were rejected under 35 USC §112, first paragraph, on the asserted grounds that the specification is not enabling with regard to R7 being taken together with R1 to form a bivalent radical. (Office Action at page 4.).

Claim 29 has been cancelled, therefore the rejection is moot as to this claim.

Claim 1 has amended to remove the possibility that formed the basis for the rejection. Therefore, the rejection has been overcome and withdrawal thereof is respectfully requested.

Obviousness Rejection

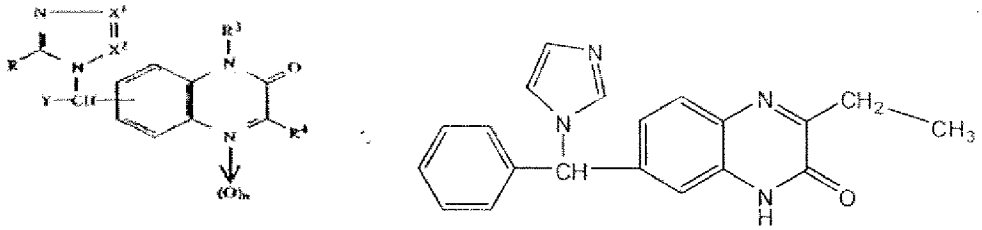
Claims 1, 6, and 29 were rejected under 35 USC §103(a) as being unpatentable over the '606 Patent. ("Office Action at page 8.)

For the reasons set forth below the rejection, respectfully is traversed.

The "606 Patent disclosure set forth in the previous paper submitted by the applicants is incorporated herein by reference.

In making the rejection, the Patent Office asserted that

> US patent 5,028,606 teaches substituted quinoxalinone derivatives (abstract and Table 9), wherein Y is Ar1 . Ar2. hydrogen: C_{1-10} alkyl: C_{3-7} cycloalkyl: C_{1-6} alkyl: C_{2-6} alkenyl or C_{2-6} alkynyl; and n is 0 or 1 and discloses the following compound (claim 1 and Table 9, compound 115):



> It further teaches that the Ar2 is phenyl substituted with 1, 2 to 3 substituents each independently selected from halo, hydroxy, trifluoromethyl, C_{1-6} alkyl, C_{1-6} alkyloxy, cyano, amino, mono- and di(C_{1-6} alkyl)amino, nitro, carboxyl, formyl and C_{1-6} alkyloxycarbonyl (column 2, line 42-49 and claim 1).
>
> The reference also teaches a pharmaceutical composition of substituted quinoxalinone derivatives with a pharmaceutically acceptable carrier (column 20, lines 47-58).

(Office Action at pages 4-5.)

The Patent Office acknowledged, however, that the '606 Patent differs from the presently claimed invention in that

> The reference does not explicitly disclose a specific embodiment wherein the phenyl ring is substituted with a substituent other than hydrogen, halo, trihalomethyl, C_{1-6} alkyl, or C_{1-6} alkyloxy although the next species is a species of the genus disclosed in US patent 5,028,606, wheerein Y is phenyl substituted with hydroxy, cyano, amino, mono- and di(C_{1-6} alkyl)amino, nitro, carboxyl, formyl and C_{1-6} alkyloxycarbonyl; n is 0; and R4 is C_{1-6} alkyl.

(Office Action at page 10.)

To fill the acknowledged gap, the Patent Office relied on mere reasoning that "the skilled chemist would have the reasonable expectation that any of the species of the genus would have similar properties and, thus, the same use as taught for the genus as a whole, i.e., pharmaceutical therapeutic agents." (Office Action at page 10.)

The Patent Office then concluded that

> One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus. *In re Susi*, 440 F.2d 442, 169 USPQ 423, 425 (CCPA 1971), followed by the Federal Circuit in *Merck & Co. v. Biocraft Laboratories*, 847 F.2d 804,

(Office Action at page 10.)

The Patent Office further found that

> . In addition, the reference already discloses the phenyl ring can be substituted with other than hydrogen, halo, trihalomethyl, C_{1-6} alkyl, or C_{1-6} alkyloxy such as hydroxy, cyano, amino, mono- and di(C_{1-6} alkyl)amino, nitro, carboxyl, formyl and C_{1-6} alkyloxycarbonyl. (Office Action at page 10.)

The Patent Office further concluded that

> it would have been prima facie obvious to one having ordinary skill in

the art at the time of the invention was made to modify the compound of US patent 5,028,606 to arrive at the claimed compound by having the phenyl ring substituted with hydroxy, cyano, amino, mono- and di(C_{1-6}alkyl)amino, nitro, carboxyl, formyl or C_{1-6}alkyloxycarbonyl because such modifications have already been suggested by US patent 5,028,606.

(Office Action at pages 10-11.)

The instant record fails to provide evidence as to whether the Patent Office considered Applicants' previous arguments. Applicants are most interested in expediting prosecution and expect the Patent Office to place in the record at least an acknowledgement that Applicants' arguments have been considered.

Claim 29 has been cancelled. Therefore the rejection as to claim 29 is moot and should be withdrawn.

It appears that the Patent Office found one of ordinary skill in the art to be a "skilled chemist." (Office Action at page 10.) However, the Patent Office did not state what the level of skill in the pertinent art would be. There are many variations and flavors of a "skilled chemist" and, it is submitted, not all "skilled chemists" would be the person of ordinary skill in art for the instant invention. In fact, it is submitted that a chemist in the pharmaceutical arts, i.e., a medicinal chemist, is the appropriate person of ordinary skill in the art. It is only when the claims are interpreted by such a person of ordinary skill that further differences between the '606 Patent and instant claims become known.

The Patent Office is again reminded that it is the claim as a whole that must be considered in making the instant rejection.

> "From the standpoint of patent law, a compound and all of its properties are inseparable; they are one and the same thing. The graphic formulae, and the chemical nomenclature, the systems of classification and study such as the concepts of homology, isomerism, etc., are mere symbols by which compounds can be identified, classified, and compared. But a formula is not a compound and while it may serve in a claim to *identify* what is being patented, as the metes and bounds of a deed identify a plot of land, the thing that is patented is not the formula but the compound identified by it."

Regents of University of New Mexico v. Knight, 321 F.3d 1111, 1122 (Fed.Cir. 2003)(Lourie, J.) (quoting *In re Papesch,* 315 F.2d 381, 391 (CCPA1963))(emphasis added).

The Patent Office should make explicit findings on the similarities and differences between the closet prior art species or subgenus of record and the claimed species or subgenus *including findings relating to* similarity of structure, *chemical properties and utilities.*(emphasis added) (MPEP 2144.08 II. A. 2 (8th ed. Rev. 6.)) It is submitted that the Patent Office failed to consider the claim as a whole to the instant facts. In fact, the Patent Office attempted to avoid the required analysis of the differences between the properties by relying on the conclusion that skilled chemists would have the responable expectation that any of the species of the genus would have similar properties and, thus, **the same use as taught for the genus as a whole, i.e, pharmaceutical therapeutic agents**." (emphasis added) (Office Action at page 10).

One of ordinary skill cannot just transpose observations for one chemical series to another totally different chemical series in the hope that it will give the same results. It all depends on the function that the particular group has in the particular compound. It is submitted that the instant facts do not provide a simple routine replacement of a methyl by ethyl as posited by the Patent Office. The position in the core structure that is the focus of the instant analysis concerns a linker between the quinoxalinone ring and the phenyl ring. It is submitted that the '606 Patent does not teach or suggest <u>any degree of freedom</u> for this modification as the Z substituent of the '606 Patent is always directly bond to the carbon atom carrying the imidazolyl. There is no disclosure or suggestion in the '606 Patent that an extra carbon atom may be inserted between the imidazolyl carrying carbon atom and the quinoxalinone moiety. Such a change would likely alter three dimensional shape of the compound.

As previously presented, the '606 patent discloses compounds that allegedly suppress plasma elimination of retinoic acids, or inhibit the formation of androgens or inhibit the action of the enzyme complex aromatase. Because of these properties, such compounds are believed to be used to treat disorders characterized by an increased proliferation and/or abnormal differentiation of epithelial cells. Therefore, these compounds have use to treat carcinomas occurring in epithelial tissues or diseases or

disorders of keratinization. They also have use in the treatment of estrogen or androgen dependent disorders such as for example breast cancer of prostatic cancer.

Contrary thereto, the compounds of the present invention have PARP inhibiting activity. Because of this activity, they have a pharmacological use on which more details are given on pages 1-5, and page 24, line 20 – page 28, line 14, of the instant specification. Among other activities, PARP inhibitors are useful to treat neural tissue damage resulting from ischemia or perfusion, to treat neurological disorders, to treat inflammation, to be used as chemosensitizers or radiosensitizers.

It is submitted that a person of ordinary skill in the art looking for PARP inhibitors, and hence compounds with a pharmacological profile of PARP inhibitors, would not have been motivated to take the '606 Patent into account. The Patent Office improperly lumped all pharmaceutical uses as being the same for purposes of providing rationale for modifying the '606 Patent. With all due respect, there are no facts in this record that a PARP inhibitor binds to the same target as compounds that suppress plasma elimination of retinoic acids, or inhibit the formation of androgens or inhibit the action of the enzyme complex aromatase. A medicinal chemist would discriminate from picking and choosing any compounds with alleged pharmafor a lead compound from which to modify.

Obviousness-type Double Patenting

Claims 1-4, 6, 14-16, and 29-30 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting. (Office Action at page 7.) The Office Action alleged that claims1-4, 6, 14-16, and 29-30 of the captioned application "are unpatentable over claims 1, 2, and 7 of co-pending US Patent Application No. 10/595,891 in view of the '606 Patent. The Office Action did not indicate that the rejected claims are otherwise allowable.

The rejection as to claim 30 is moot in view of the cancellation of claim 30 and withdrawal of the rejection is respectfully requested.

Upon notification in the Office Action that claims 1-4, 6, are 14-16 allowable but for this rejection, the substance of this rejection will be addressed.

Finally, the Examiner is invited to call the applicants' undersigned representative if any further action will expedite the prosecution of the application or if the Examiner

has any suggestions or questions concerning the application or the present Response. In fact, if the claims of the application are not believed to be in full condition for allowance, for any reason, the applicants respectfully request the constructive assistance and suggestions of the Examiner in drafting one or more acceptable claims pursuant to MPEP § 707.07(j) or in making constructive suggestions pursuant to MPEP § 706.03 so that the application can be placed in allowable condition as soon as possible and without the need for further proceedings.

Accordingly, entry of the claims and allowance of the claims is respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

Respectfully submitted,

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